(Submitted via Internet November 12, 2001)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Dipropylene Glycol Benzoate.

The testing plan for dipropylene glycol benzoate (DGDB), also known as benzoflex, submitted by Velsicol proposes no new testing. We agree that the database for ecological and health endpoints is adequate for screening-level purposes, and that no further testing is needed within the context of the High Production Volume (HPV) initiative. However, we do have concerns regarding the positive results found in the developmental toxicity studies, which were conducted only in rats; we urge that additional developmental studies on mice be regarded as a high priority for post-HPV purposes. It may be appropriate to combine these studies with repeat-dose studies. (Initiation of such studies need not, and indeed should not, await completion of the entire HPV initiative.)

Specific comments are as follows:

1. DGDB is widely used as a plasticizer in latex caulks and sealants, in vinyl flooring, and in numerous other products that offer the opportunity for exposure of a wide segment of the population including children and women of childbearing age. Therefore it is important that the toxicological database is sufficiently strong to support definitive safety assessments. While the HPV program does not seek to provide this type of definitive assessment, it may - as in this instance - point to high-priority needs for follow-up testing.

2. Although exposure assessments are not required under the HPV program, the wide use of DGDB in household products raises the issue of real life exposures as determined by blood or urine monitoring. Recent data generated by CDC revealed that some phthalate acid plasticizers were found in much-higher-than-expected levels in people including women of childbearing age. We are not aware that human exposure data are available for DGDB.

3. Acute toxicity data in male and female animals are sufficient.

4. Genetic toxicity tests in multiple systems are adequate to conclude that DGDB possesses no or very weak genetic toxicity activity.

5. Repeat dose toxicity studies were conducted in rats. These studies employed treatment of animals for 13 weeks and were used to establish a NOAEL of 1000 mg/kg/day, demonstrating that DGDB exhibits low toxicity following chronic exposures. Although plasma cholesterol levels were elevated at doses as low as 100 mg/kg/day, this effect was not dose related and was not accompanied by liver toxicity even at much higher doses. Given the opportunity for human exposure to DGDB and the fact that significant species differences are known to occur in toxicity studies, some consideration should be given to the need for conducting repeat dose studies in mice, particularly if these can be combined with developmental toxicity studies as noted below.

6. Developmental toxicity studies were conducted in rats. Velsicol claims a No Observed Effect

Level (NOEL) of 1000 mg/kg, for exposures between days 6 and 19 of gestation, based on a small but significant increase in the number of cervical ribs. The data presented in the summaries showed a notable increase at 1000 mg/kg but not at 500 mg/kg, so that the NOEL should be 500 mg/kg. Although the studies in rats were conducted according to established guidelines, we note that the concordance between rats and mice for developmental toxicity studies is poor (in the range of 50%). Since there is clear potential for exposure of women of childbearing age to DGDB, we recommend that developmental toxicity studies be conducted in mice. These data are necessary for a credible and complete safety assessment at the post-HPV stage.

7. Reproductive toxicity studies were conducted in rats according to established guidelines employing appropriate doses. These studies were essentially negative and are sufficient to conclude that DGDB does not pose reproductive risks to people under expected exposure circumstances. Unlike the situation for developmental toxicity studies, the toxicological community generally agrees that rat studies are adequate for safety and risk assessments so studies in mice are not needed.

Thank you for this opportunity to comment.

George Lucier, Ph.D.
Consulting Toxicologist, Environmental Defense

Karen Florini
Senior Attorney, Environmental Defense